DRAFT STATUTORY INSTRUMENTS

2019 No.

The Human Medicines (Amendment etc.) (EU Exit) Regulations 2019

PART 11

Amendment of Part 11 (Pharmacovigilance)

Amendment of regulation 177 (application of Part and interpretation)

139.—(1) Regulation 177(**1**) is amended as follows.

(2) In paragraph (1)—

(a) for "Schedule 33", substitute "Schedules 12A and 33";

(b) omit ", except to the extent set out in paragraph (4)(b),";

(c) in sub-paragraph (a), at the end insert "or";

(d) omit sub-paragraph (c) (and "or" immediately preceding it).

(3) In paragraph (2)—

(a) after "this Part" insert "and Schedule 12A";

(b) in sub-paragraph (a), insert "or" at the end;

(c) omit sub-paragraph (c) (and "or" immediately preceding it).

(4) In paragraph (3)—

(a) for "Schedule 33" substitute "Schedules 12A and 33";

(b) in sub-paragraph (a), at the end insert "or";

(c) omit sub-paragraph (c) (and "or" immediately preceding it).

(5) Omit paragraph (4).

(6) In paragraph (5), omit the definitions of "co-ordination group", "Eudravigilance database", "Implementing Regulation" and "relevant competent authorities".

Amendment of regulation 180 (obligation on licensing authority to audit pharmacovigilance system)

140.—(1) Regulation 180 is amended as follows.

(2) In paragraph (1), omit "and report the results of that audit to the European Commission".

(3) In paragraph (2)—

(a) omit "results of the"; and

(b) for "reported to the European Commission" substitute "performed".

(**1**) Regulation 177 was amended by S.I. 2013/1855 and 2014/1878.

Omission of regulation 181 (delegation of obligations under Part 11)

141. Omit regulation 181.

Amendment of regulation 182 (obligation on holder to operate a pharmacovigilance system)

142.—(1) Regulation 182(**2**) is amended as follows.

(2) In paragraph (2)(a), for "resides and operates in the EU" substitute "is ordinarily resident, and operates, in the United Kingdom".

(3) In paragraph (3), insert at the beginning "Without prejudice to the requirements set out in regulation 65C and Schedule 10A (variations to a UK marketing authorisation)".

(4) Omit paragraph (6).

Amendment of regulation 184 (obligation on holder to audit pharmacovigilance system)

143. In regulation 184, after paragraph (2) insert—

"(3) The holder must also comply with the requirements of paragraph 13 of Schedule 12A in relation to auditing the pharmacovigilance system.".

Amendment of regulation 185 (recording obligations on the licensing authority)

144. In regulation 185(b), after "by" insert "a holder,".

Amendment of regulation 186 (reporting obligations on the licensing authority)

145. In regulation 186(1)—

(a) at the end of sub-paragraph (a) insert "and"; and

(b) omit sub-paragraphs (c) to (e).

Insertion of new regulation 187A (collaboration with the World Health Organisation)

146. After regulation 186 insert—

"**186A.** The licensing authority must collaborate with the World Health Organisation in matters of pharmacovigilance, and must in particular—

(a) take the necessary steps to promptly submit to the World Health Organisation appropriate and adequate information regarding the measures taken in the United Kingdom which may have a bearing on public health protection in other countries; and

(b) make available promptly all suspected adverse reaction reports occurring in the United Kingdom to the World Health Organisation.".

Amendment of regulation 187 (recording obligations on holders)

147.—(1) Regulation 187 is amended as follows.

(2) In paragraph (1), for "in the EEA or in third countries" substitute "in the United Kingdom or another country".

(3) In paragraph (4), for "EEA" substitute "United Kingdom".

(**2**) Regulation 182 was amended by S.I. 2013/1855.

Amendment of regulation 188 (reporting obligations on holders)

148.—(1) Regulation 188 is amended as follows.

(2) In each place where it occurs, for "Eudravigilance database" substitute "licensing authority".

(3) In paragraph (1)—

(a) in sub-paragraph (a)—

(i) for "EEA" substitute "United Kingdom", and

(ii) for "third countries" substitute "countries other than the United Kingdom";

(b) in sub-paragraph (b), for "EEA" substitute "United Kingdom";

(c) in sub-paragraph (e), for "EMA and the competent authorities of the EEA States" substitute "licensing authority".

(4) Omit paragraphs (2) and (3).

(5) In paragraph (4)(a), omit "other than monitored publications".

(6) In paragraph (5), omit the definitions of "monitored active substance" and "monitored publication".

(7) Omit paragraph (6).

Amendment of regulation 189 (signal detection: licensing authority obligations)

149.—(1) Regulation 189 is amended as follows.

(2) In paragraph (1)—

(a) in sub-paragraph (a), for "in the Eudravigilance database" substitute "that it collects by virtue of operating its pharmacovigilance system under this Part"; and

(b) in sub-paragraph (d), for "regulations 59 to 61" substitute "regulations 59, 60 and 61".

(3) Omit paragraphs (2) to (4).

Amendment of regulation 190 (signal detection: holder obligation)

150. In regulation 190(1), omit "the EMA and".

Amendment of regulation 191 (obligation on holder to submit periodic safety update reports: general requirements)

151.—(1) Regulation 191 is amended as follows.

(2) In paragraphs (1) and (7), for "EMA" substitute "licensing authority".

(3) In paragraph (2), insert "UK" before "marketing authorisation".

(4) In paragraph (3), omit—

(a) "or an Article 126a authorisation" in both places it appears; and

(b) "or Article 126a authorisation".

(5) After paragraph (4) insert—

"(4A) A PSUR must also include the content, and be submitted in the format, specified in Part 8 of Schedule 12A.".

(6) After paragraph (8), insert—

"(8A) In the case of a conditional marketing authorisation, the holder must submit PSURs immediately upon the request of the licensing authority and at least every six months

beginning with the date on which the authorisation for the medicinal product is granted or renewed by the licensing authority.".

(7) In paragraph (10), for "within the EEA" in each place it appears substitute "in the United Kingdom".

(8) Omit paragraph (11).

Amendment of regulation 192 (obligation to submit periodic safety reports: derogation from general requirements)

152.—(1) Regulation 192 is amended as follows.

(2) In paragraph (1)(a), insert "UK" before "marketing authorisation".

(3) In paragraph (3), for "EMA" substitute "licensing authority".

(4) Omit paragraphs (9) to (11).

Amendment of regulation 193 (harmonisation of PSUR frequency or date of submission)

153.—(1) Regulation 193 is amended as follows.

(2) Omit paragraph (1)(a).

(3) For paragraph (2) substitute—

"(2) Where one or more of the grounds in paragraph (3) is met, the holder may submit a request in writing to the licensing authority, or the licensing authority may in any event decide, to—

(a) determine a UK reference date from which submission dates are calculated in respect of products that fall under paragraph (1); or

(b) change the frequency and date of submission of the PSUR.".

(4) For paragraph (4) substitute—

"(4) Where the licensing authority makes a decision under paragraph (2) following a written request from a holder, it must notify that holder in writing of its decision to approve or refuse the request.".

(5) In paragraph (5)—

(a) for "Article 107c(4) or Article 107c(6) of the 2001 Directive" substitute "paragraph (2)"; and

(b) for "EMA" substitute "licensing authority".

(6) For paragraph (6) substitute—

"(6) Subject to paragraph (6A), in this regulation, "UK reference date" means a date determined by the licensing authority under paragraph (2)(a) in respect of medicinal products containing the same active substance or the same combination of active substances.

(6A) Until the licensing authority makes a decision under paragraph (2), any—

(a) Union reference date in respect of medicinal products containing the same active substance or the same combination of active substances; or

(b) date of submission and frequency of periodic safety reports in respect of such products,

published by the EMA under Article 107c(7) of the 2001 Directive, is deemed to be the UK reference date or, as the case may be, the required date or frequency of PSUR submission, in respect of those medicinal products.".

(7) After paragraph (6A) insert—

"(7) The licensing authority must publish a list of—

(a) UK reference dates it determines under paragraph (2); and

(b) the required date of submission and frequency for PSURs in respect of medicinal products containing the same active substance or the same combination of active substances.

(8) Any change to the date of submission and frequency of PSURs as a result of the application of this regulation is to take effect after a 6 month period, such period beginning with the day after the licensing authority publishes that change under paragraph (7).".

Omission of regulation 194 (responding to a single assessment of PSUR under Article 107e of the 2001 Directive)

154. Omit regulation 194.

Amendment of regulation 195 (obligation on licensing authority to assess PSURs)

155.—(1) Regulation 195(**3**) is amended as follows.

(2) In the heading, omit "where EU single assessment procedure does not apply".

(3) For paragraph (1) substitute—

"(1) This regulation applies where PSURs relating to a medicinal product have been submitted to the licensing authority under regulations 191 to 192.".

(4) After paragraph (3) insert—

"(3A) If the licensing authority considers under paragraph (3)(b) that an authorisation or registration needs to be varied, it may require the holder to submit to the licensing authority, within a time period that the licensing authority specifies, an application for a variation, including—

(a) an updated summary of the product characteristics; and

(b) an updated package leaflet.".

(5) In paragraph (4), omit the definitions of "EU reference date" and "EU single assessment procedure".

Substitution of regulation 196 (urgent action)

156. For regulation 196(**4**) and the italic heading immediately preceding it substitute—

"Major safety review

Major safety review by the licensing authority

196.—(1) The licensing authority may conduct a major safety review where—

(a) on the basis of concerns resulting from the evaluation of data from pharmacovigilance activities it considers—

(i) suspending or revoking a UK marketing authorisation or traditional herbal registration of a medicinal product or in respect of a class of medicinal products,

(**3**) Regulation 195 was amended by S.I. 2014/1878.
(**4**) Regulation 196 was amended by S.I. 2013/2593.

(ii) prohibiting the supply of a medicinal product or a class of medicinal products,

(iii) refusing the renewal of a UK marketing authorisation or traditional herbal registration, or

(iv) action is necessary to vary a UK marketing authorisation or traditional herbal registration or a class of such authorisations or registrations, including to impose new conditions; or

(b) it is informed by a holder that, on the basis of safety concerns, the holder has—

(i) interrupted the sale or supply, or offer of sale or supply, of the product to which a UK marketing authorisation or traditional herbal registration relates,

(ii) taken action to have that product's authorisation or registration cancelled or intends to do so, or

(iii) not applied for the renewal of that product's authorisation or registration.

(2) If the licensing authority conducts a review under paragraph (1), it must—

(a) announce the initiation of that review on the UK web-portal as soon as reasonably practicable;

(b) include in that announcement—

(i) an outline of its reasons for conducting a major safety review, the medicinal products concerned and, where applicable, the active substances concerned, and

(ii) the proposed structure and time-scale of the review;

(c) notify a holder if the product to which that holder's authorisation or registration relates is within the scope of the review; and

(d) publish the outcome of that review, including any recommendations it is making, or action it is proposing to take, as soon as reasonably practicable after the conclusion of that review.

(3) A holder who is notified under paragraph (2)(c)—

(a) must provide to the licensing authority such information as the licensing authority notifies that holder it requires, within such time period as the licensing authority specifies; and

(b) may, where such information contains confidential data relevant to the subject matter of the review, because the data relates to a manufacturing process or trade secret, notify the licensing authority that that data is provided in confidence.

(4) Where the licensing authority proposes that action should be taken in respect of any UK marketing authorisation or traditional herbal registration—

(a) during the conduct of the major safety review, because urgent action is necessary to protect public health; or

(b) upon the conclusion of such a review,

it may exercise its powers under Part 5 or 7 (as the case may be) in relation to that authorisation or registration.".

Omission of regulation 197 (EU urgent action procedure)

157. Omit regulation 197.

Amendment of regulation 198 (post-authorisation safety studies: general provisions)

158.—(1) Regulation 198 is amended as follows.

(2) In paragraph (2), for "competent authorities of the EEA States in which the study is conducted" substitute "licensing authority".

(3) In paragraph (3)—

(a) in sub-paragraph (c), for "relevant competent authorities" substitute "licensing authority";

(b) in sub-paragraph (d), for "competent authorities of the EEA States in which the study was conducted" substitute "the licensing authority if the study is conducted in the United Kingdom".

Amendment of regulation 199 (submission of draft study protocols for required studies)

159.—(1) Regulation 199 is amended as follows.

(2) In paragraph (2), for "body specified in paragraph (3)" substitute "licensing authority".

(3) Omit paragraphs (3) and (4).

(4) In paragraph (5), omit "Where this paragraph applies".

(5) In paragraph (6), omit sub-paragraph (b) (and "or" immediately preceding it).

(6) Omit paragraphs (7) and (8).

Amendment of regulation 200 (amendment to study protocols for required studies)

160.—(1) Regulation 200 is amended as follows.

(2) In paragraph (2), for "body specified in paragraph (3)" substitute "licensing authority".

(3) Omit paragraphs (3) and (4).

(4) In paragraph (5), omit "Where this paragraph applies".

(5) Omit paragraphs (6) and (7).

Amendment of regulation 201 (submission and evaluation of final study reports for required studies)

161.—(1) Regulation 201 is amended as follows.

(2) In paragraph (2), for "body specified in paragraph (3)" substitute "licensing authority".

(3) Omit paragraph (3).

(4) In paragraph (4), omit from "for reports" where it first appears to the end.

Omission of regulation 202 (follow up of final study reports)

162. Omit regulation 202.

Insertion of new regulation 202A (medicinal products subject to additional monitoring)

163. After regulation 202 insert—

"Medicinal products subject to additional monitoring

Licensing authority power in relation to medicinal products subject to additional monitoring

202A.—(1) The licensing authority may establish a list of medicinal products that are subject to additional monitoring.

(2) The list referred to in paragraph (1) is to include the names and active substances of—

(a) medicinal products authorised in the United Kingdom that contain a new active substance which, on 1st January 2011, was not contained in any medicinal product authorised in the United Kingdom;

(b) any biological medicinal product not covered by sub-paragraph (a) that was authorised in the United Kingdom after 1st January 2011;

(c) medicinal products that are authorised pursuant to these Regulations, subject to the conditions referred to in regulation 50I, 59(2)(b) or (c), 60 or 61(4).

(3) If the licensing authority considers it appropriate, medicinal products that are authorised pursuant to these Regulations, subject to the conditions referred to in regulation 59(2)(a), (d), (e) or (f), 61(5) or 183(2), may also be included in the list referred to in paragraph (1).

(4) For medicinal products included in the list referred to in paragraph (1)—

(a) the summary of product characteristics and the package leaflet must include a symbol and statement as follows: "▼ This medicinal product is subject to additional monitoring"; and

(b) that symbol must be proportional to the font of the subsequent standardised text, and each side of the triangle must have a minimum length of 5 millimetres.

(5) In the cases referred to in paragraph (2)(a) and (b), the licensing authority must, unless paragraph (6) applies, remove a medicinal product from the list after five years, beginning with the day after the UK reference date referred to in regulation 193.

(6) In the cases referred to in paragraph (2)(c) and (3), the licensing authority must remove a medicinal product from the list once the condition or obligation under a provision specified in those paragraphs has been fulfilled.

(7) Until the licensing authority publishes a list of medicinal products under paragraph (1), the reference to that list is instead to be read as a reference to the list referred to in Article 23 of Regulation (EC) No 726/2004, as that list may be amended from time to time.".

Amendment of regulation 203 (obligations on licensing authority in relation to national medicines web-portal)

164.—(1) Regulation 203 is amended as follows.

(2) In paragraph (1), omit from "linked" to the end.

(3) In paragraph (2)—

(a) in sub-paragraph (e) for "Article 23 of Regulation (EC) No 726/2004" substitute "the list published by the licensing authority under, or which applies by virtue of, regulation 202A"; and

(b) in sub-paragraph (f), omit "(including by way of the web-based forms referred to in Article 25 of Regulation (EC) No 725/2004".

Omission of regulation 204 (obligation on licensing authority in relation to public announcements)

165. Omit regulation 204.

Amendment of regulation 205 (obligations on holders in relation to public announcements)

166.—(1) Regulation 205 is amended as follows.

(2) In paragraph (2), for "bodies listed in paragraph (3)" substitute "licensing authority".

(3) Omit paragraph (3).

Insertion of regulation 205A (further obligations in respect of pharmacovigilance activities)

167. After regulation 205 insert—
"Further obligations in respect of pharmacovigilance activities

Further obligations in respect of pharmacovigilance activities

205A.—(1) Schedule 12A makes further provision as to the obligations of a holder and the licensing authority in respect of the performance of pharmacovigilance activities under this Part.

(2) The Ministers may by regulations amend Schedule 12A.

(3) Regulations under paragraph (2) may make provision regarding the performance of pharmacovigilance activities under this Part as to—

(a) the content and maintenance of the pharmacovigilance system master file kept by the holder;

(b) the minimum requirements for the quality system for the performance of pharmacovigilance activities by the holder and the licensing authority;

(c) the use of internationally agreed terminology, formats and standards for the performance of pharmacovigilance activities;

(d) the minimum requirements for the monitoring of data recorded by the licensing authority pursuant to regulation 185 (recording obligations on the licensing authority) to determine whether there are new risks or whether risks have changed;

(e) the format and content of electronic transmission of suspected adverse reactions by a holder;

(f) the format and content of electronic periodic safety reports and risk management plans; and

(g) the format of protocols, abstracts and final study reports for the post-authorisation safety studies.".

Insertion of new Schedule 12A (further provision as to performance of pharmacovigilance activities)

168. Schedule 6 inserts a new Schedule 12A after Schedule 12 to the 2012 Regulations.

Insertion of regulation 205B (guidance in respect of good pharmacovigilance practice and post authorisation efficacy studies)

169. After new regulation 205A insert—

"Guidance in respect of pharmacovigilance

Guidance in respect of good pharmacovigilance practice and post authorisation efficacy studies

205B.—(1) The licensing authority may publish—

(a) guidance on good pharmacovigilance practices for both the licensing authority and UK marketing authorisation holders;

(b) scientific guidance on post authorisation efficacy studies.

(2) Subject to paragraph (3), the guidance issued by the Commission under Article 108a of the 2001 Directive on the matters specified in paragraph (1)(a) and (b) continues to apply until the date on which the licensing authority publishes guidance under paragraph (1).

(3) The licensing authority—

(a) may determine that provisions of the guidance specified in paragraph (2) no longer apply, or apply subject to specified modifications, from a date that it specifies; and

(b) must, if it so determines, publish its determination.

(4) Guidance published under paragraph (1), or which applies by virtue of paragraph (2) (as modified by any determination under paragraph (3), as the case may be), is to be taken into account in consideration of whether there has been any failure to comply with a provision in this Part, or Schedule 12A, to which the guidance is relevant.".

Amendment of regulation 206 (infringement notices)

170.—(1) Regulation 206(**5**) is amended as follows.

(2) In paragraph (1)—

(a) omit "relevant"; and

(b) after "provision" insert "of this Part or Schedule 12A ("relevant provision").

(3) Omit paragraphs (3) and (4).

Amendment of regulation 207 (offences)

171. In regulation 207(1), after "other than" insert "Schedule 12A (further requirements in respect of pharmacovigilance activities) and".

Amendment of regulation 208 (false and misleading information)

172. In regulation 208, omit "or the EMA".

Amendment of regulation 209 (penalties)

173. In regulation 209(3), omit sub-paragraphs (h) and (i).

Omission of regulation 210 (offences relating to pharmacovigilance obligations under Regulation (EC) No 726/2004)

174. Omit regulation 210(**6**).

(**5**) Regulation 206 was amended by S.I. 2013/1855.
(**6**) Regulation 210 was amended by S.I. 2013/1855.

Amendment of regulation 210A (offences in relation to pharmacovigilance obligations under the Implementing Regulation)

175.—(1) Regulation 210A(**7**) is amended as follows.

(2) In the heading, for "the Implementing Regulation" substitute "Schedule 12A".

(3) In paragraph (1)—

(a) in sub-paragraph (a) for "the Implementing Regulation" substitute "Schedule 12A"; and

(b) in sub-paragraph (b)—

(i) for "the Implementing Regulation" substitute "Schedule 12A", and

(ii) omit "or the EMA".

(4) For paragraph (2) substitute—

"(2) The provisions of Schedule 12A mentioned in paragraph (1)(a) are—

(a) Part 1 (pharmacovigilance system master file);

(b) Parts 2 and 3 (minimum requirements for the quality systems in the performance of pharmacovigilance activities);

(c) Part 6 (transmission of reports of suspected adverse reactions);

(d) paragraph 24 (update of risk management plans);

(e) Part 8 (periodic safety update reports); and

(f) Part 9 (post-authorisation safety studies).

(3) Subject to paragraph (4), a person guilty of an offence under this regulation is liable—

(a) on summary conviction to a fine not exceeding the statutory maximum; or

(b) on conviction on indictment to a fine.

(4) A person guilty of an offence under this regulation which relates to a breach of paragraph 26(8) or 29(1) of Schedule 12A is liable—

(a) on summary conviction to a fine not exceeding the statutory maximum; or

(b) on conviction on indictment to a fine, to imprisonment for a term not exceeding two years or to both.".

Amendment of regulation 211 (persons liable)

176. In regulation 211, omit from first "or" to "No 726/2004)".

Amendment of regulation 212 (transitional arrangements)

177. In regulation 212, for "182, 186, 188, 191, 192, 198, 199, 200, 201, 202 and 210" substitute "198, 199, 200, 201 and 202".

Amendment of Schedule 33 (transitional arrangements: pharmacovigilance)

178. In Schedule 33, omit paragraphs 1, 2 and 4 to 10.

(**7**) Regulation 210A was inserted by S.I. 2013/1855.